

## REMARKS

Claims 1-8, 10 and 14 are pending. By the present amendment, claims 1 and 14 are amended.

Support for the amendments to claims 1 and 14 can be found in the specification at, for example, page 43, lines 16-22 or the paragraph spanning pages 71-72. The amendments do not introduce any new matter.

The insertion of “plant selection strategy” in the preamble of Claims 1 and 14 is to provide an antecedent basis for the wherein clause; it does not raise a new issue or require a new search. The amendments of Claims 1 and 14, which recite (i) wherein expression of the first nucleotide sequence is benign to the plant or portion thereof, and (ii) wherein the plant selection strategy method confers no adaptive advantage, is benign to the plant or portion thereof, and is not based on antibiotic resistance, are made in response to the Final Office Action. The amended phrases were searched before in the previous Office Action, thus the amendments do not raise a new issue or require a new search.

The amendments are necessary to put the claims in a form for allowance or in a better form for appeal. The Examiner is requested to enter the amendments and re-consider the application.

### CLAIM REJECTIONS - 35 U.S.C. § 112, First Paragraph

Claims 1-8, 10 and 14 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. More specifically, the Office Action alleges that the recitation of “the first, second and third coding regions encode proteins that confer no adaptive advantage, are benign to the plant, and are not antibiotic resistant” in claim 1 adds new matter. It is further alleged that the specification only supports that the selection marker genes are otherwise benign and confer no adaptive advantage.

The Applicant respectfully submits that these phrases are not new matter and are supported in the specification at, for example, page 43, lines 16-22 or at the paragraph bridging pages 71-72. To expedite prosecution, independent claims 1 and 14 have been amended to recite that the claimed methods comprise a plant selection strategy that confers no adaptive advantage, is benign to the plant, and is not based on antibiotic resistance. This amendment is clearly supported at page 43, lines 16-22 of the specification, where it is

disclosed:

*An aspect of the present invention therefore provides a plant selection strategy to identify and select plants cells, tissue or entire plants which comprise a coding region of interest (70). The plant selection strategy exemplified by the various aspects of embodiments discussed above need not be based on antibiotic resistance. Further, the plant selection strategy is benign to the transformed plant and confers no advantage to other organisms in the event of gene transfer. The present invention also provides genetic constructs which may be employed in plant selection strategies.*

Claims 1 and 14 have been further amended to recite that expression of the first nucleotide sequence is benign to the plant or portion thereof. In the present invention, the first nucleotide sequence containing the first coding region encoding a repressable tag protein, can be introduced into a transgenic plant or portion thereof to obtain a plant platform for subsequent transformation with the second nucleotide sequence as is disclosed in Example 5, and on page 37, lines 6-28, and page 39, lines 28-32 of the specification. It is therefore implicit from the teaching of the specification that expression of the first nucleotide sequence is benign to the plant in order that the first nucleotide sequence can be introduced into the plant to obtain a plant platform for subsequent transformation with the second nucleotide sequence.

It is stated in the Office Action that the specification only supports that the selection marker genes are otherwise benign and confer no adaptive advantage. Applicant submits that the Examiner is misunderstanding the teaching of the specification, for example it is disclosed in the paragraph bridging pages 71-72 of the specification:

*The present invention provides a selectable marker system that allows the efficient selection of transformed plants utilizing genes that are otherwise benign and confer no adaptive advantage. The benign selectable marker system may facilitate public acceptance of genetically modified organisms by eliminating the issue of antibiotic resistance. Further, the present invention provides a selectable marker system for plant transformation that includes stringent selection of transformed cells, avoids medically relevant antibiotic resistance genes, and*

*provides an inexpensive and effective selection agent that is not-toxic to plant cells.*

As disclosed in the specification, the present invention provides a selectable marker system which does not rely on antibiotic resistance genes, is benign to the plant and confers no adaptive advantage. As the first nucleotide sequence is part of the selectable marker system of the present invention, it follows that expression of the first nucleotide sequence is benign to the plant or portion thereof.

In *Martek Biosciences v. Nutrinova and Lonza* (Fed. Cir. 2009) with regards to the written description requirement for new matter it was held "the earlier application need not describe the claimed subject matter in precisely the same terms as found in the claim." *Tech Licensing* (Fed. Cir. 2008). Rather, the test is "whether the disclosure of the application relied upon reasonably conveys to the artisan that the inventor had possession at that time of the later claimed subject matter." Applicants submit that the disclosure of the present application reasonably conveys to the artisan that the inventor had possession at the time of the presently claimed feature "expression of the first nucleotide sequence is benign to the plant or portion thereof".

Applicants respectfully request that the rejection to claims 1-8, 10 and 14 under 35 U.S.C. § 112, first paragraph be reconsidered and withdrawn.

#### **CLAIM REJECTIONS - 35 USC § 103(a)**

Claims 1-8, 10 and 14 remain rejected under 35 U.S.C. §103(a) as being unpatentable over Fabijanski et al. in view of Mason et al. and Chou et al.

The Office Action contends that even if the method Fabijanski et al. may be designed for different purpose, Fabijanski et al. in view of Mason et al. and Chou et al. teach all the steps of instant invention. The Office Action further contends that Fabijanski et al. teach a second nucleotide sequence comprising a new trait sequence (corresponding to a second regulatory region in operative association with a second coding region) and repressor 2 gene (corresponding to a third coding region encoding a repressor capable of binding to the operator sequence thereby inhibiting expression of the first coding region) (Figure 3). Further, Fabijanski et al. also teach using oncogene 1 and 2 as a selection marker (Example 5, columns 33-35; also Table 1) which is similar to the conditionally lethal gene, *iaaH*, as

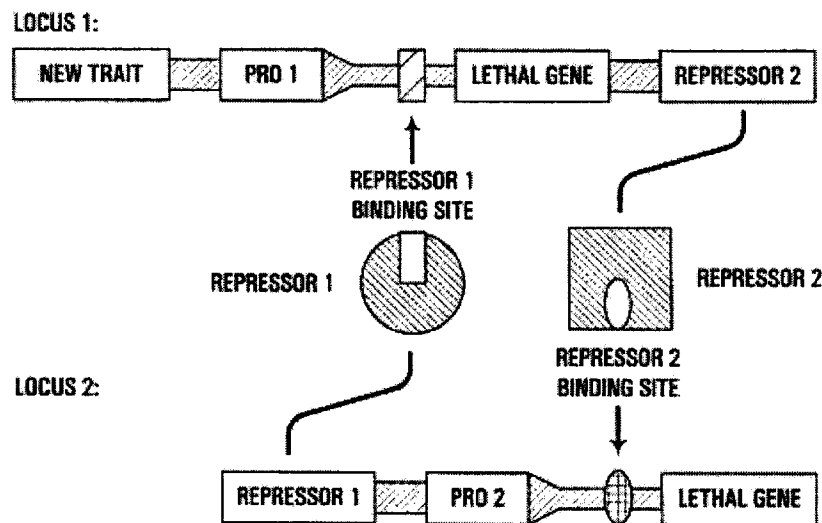
disclosed in Example 5 of the instant specification. Therefore, Fabijanski et al. teach a selection strategy that is benign to the plant. Applicants respectfully disagree.

Applicant submits that Fabijanski et al. not only teach a method that is designed for a different purpose when compared to the methods as claimed in the present invention, but also, that the combination of components of the constructs taught in Fabijanski et al. are different from the combination of components in the constructs claimed in the present invention.

In the plant selection strategy method of claims 1 and 14, expression of the first nucleotide sequence is benign to the plant or portion thereof. By benign, it is meant that the first nucleotide sequence when expressed is non-toxic and confers no adaptive advantage to the plant (see paragraph spanning pages 71-72 of the specification). Furthermore, the selection strategy is not based on antibiotic resistance.

Examiner stated in the previous office action that Fabijanski et al. teach DNA constructs of Figure 3, wherein locus 2 (corresponding to first nucleotide sequence in the instant claims) containing a lethal gene (corresponding to tag gene) under the control of a modified repressible promoter, Pro2 (corresponding to first regulatory region).

Figure 3 of Fabijanski et al. is reproduced below:



**Both constructs in Fabijanski et al. encode a repressor and they both encode a lethal gene product.** As disclosed at column 15, lines 24-38 of Fabijanski et al.:

*methods and compositions are provided for a novel means of producing transgenic plants that contain two recombinant repressible lethal gene constructs. All plants comprising recombinant DNA resulting from outcrossing of the transgenic plant are rapidly eliminated from the environment. The first repressible lethal gene construct comprises a lethal gene and a repressor gene that blocks the expression of a second repressible lethal gene and optionally a gene encoding a novel trait of interest. The second repressible lethal gene construct comprises a second lethal gene and a repressor gene that blocks the expression of the first repressible lethal gene. Cells containing both genetic constructs produce two types of repressor molecules; hence both lethal genes remain in a repressed state.*

Thus there is no hint or suggestion in Fabijanski et al. that expression of the first nucleotide sequence (which corresponds to Locus 2 in Fabijanski) is benign to the plant or portion thereof as is claimed in amended claims 1 and 14.

It is alleged in the Office Action that Fabijanski et al. teach using oncogene 1 and 2 as a selection marker (Example 5, columns 33-35; also Table 1) which is similar to the conditionally lethal gene, *iaaH*, as disclosed in Example 5 of the instant specification. Applicants submit that Example 5 of Fabijanski et al. teaches crossing a plant that contains a repressible seed lethal gene (plant A) with a plant that contains a repressor gene (plant B) to obtain plant C. As shown in Table 1 of Fabijanski et al., and disclosed at column 34, lines 62-65 “[n]o plants were recovered that carried a seed lethal gene, proving that without the presence of a repressor no viable plants can be formed from seeds with a seed lethal genotype.” **Thus expression of the first nucleotide sequence containing the first coding region encoding a repressable tag protein is not benign to the plant, but instead results in a non-viable plant.**

Example 3 of Fabijanski et al. (column 31, line 45 to column 32, line 32) discloses a plant transformation vector which comprises a repressible lethal gene activity resulting from the combined activity of two genes, oncogene 1 and native oncogene 2. It is disclosed “[w]hen expressed, the two oncogenes in this vector lead to the formation of excess IAA, killing plant cells in which the lethal gene activity is expressed.” It is taught in Fabijanski et al. that the Binter vector “containing the Xba

I fragment comprising the phaseolin promoter... the coding region of oncogene 1... and the native oncogene 2” is referred to as pGG-2. In Example 4 of Fabijanski et al. (column 32, line 33 to column 33, line 16) tobacco plants are transformed with the vector pGG-2 to obtain plants which comprise a repressible seed lethal gene activity, “[t]obacco plants that carry the repressible seed lethal gene but do not carry a repressor form seeds that are not viable”. Fabijanski et al. therefore teaches that oncogene 1 and oncogene 2 are both expressed on the same nucleotide sequence (equivalent to the first nucleotide sequence of the present invention) and the combined expression of both genes is lethal to the plant. Thus expression of the first nucleotide sequence containing the first coding region encoding a repressable tag protein is **not** benign to the plant, but instead results in a non-viable plant.

**Oncogene 1 and oncogene 2 of Fabijanski et al. do not work in the same way as conditionally lethal gene, *iaaH* as disclosed in Example 5 of the present application.** In Example 5 of the present application, the first nucleotide sequence comprises an *iaaH* gene (first coding region) linked to a constitutive promoter altered to incorporate the DNA binding sites (operator sequence) for a transcriptional repressor protein, “[w]hen introduced into a transgenic plant, the resultant line is sensitized to IAM exposure, or its analogues, as this chemical is converted to IAA causing aberrant cell growth and eventual death of the plant”. As disclosed at page 21, lines 26-29 of the present specification “IAAH (tms2) converts the non-toxic substrates indole acetamide (IAM), or indole naphthalacetimide (NAM), to indole acetic acid (IAA; Figure 1), or indole naphthal acetic acid (NAA), respectively. The products, IAA or NAA, are toxic at elevated concentrations within a plant or portion thereof”. Therefore, expression of the first nucleotide containing the conditionally lethal gene *iaaH* in Example 5 is benign to the plant, however the plant is sensitized to exposure to the non-toxic substrates indole acetamide (IAM), or indole naphthalacetimide (NAM). This is very different to expression of the construct in Fabijanski et al. containing oncogene 1 and oncogene 2, as the combined expression of these genes is lethal to the plant.

In the present invention, the first nucleotide sequence containing the first coding region encoding a repressable tag protein that is benign to the plant or portion thereof when expressed, can be introduced into a transgenic plant or portion thereof to obtain a plant

platform for subsequent transformation with the second nucleotide sequence as is disclosed in Example 5 of the present application. Unlike the system taught in Fabijanski et al., there is no need for both the first and second nucleotide sequences to be introduced into the transgenic plant at the same time to ensure that the first coding region (lethal gene) is repressed to allow the plant to survive.

The Applicants respectfully submit that Fabijanski et al. teaches away from the present invention. The plant selection strategy method of Claims 1 and 14 enables a plant platform that has been transformed with the first nucleotide sequence to be produced for subsequent transformation with a second nucleotide sequence comprising a second coding region comprising a coding region of interest and a third coding region encoding a repressor. **Fabijanski et al. teaches that whenever the first nucleotide sequence is expressed without the second nucleotide sequence, the plant is not viable.**

Furthermore, Fabijanski et al. do not teach antibiotic resistance as an undesirable feature, as is presently claimed. Rather, the pCG-2 transformation vector (which contains the Oncogene 1 and 2 sequences) taught by Fabijanski et al. includes a kanamycin resistance gene (col. 32, ll 60-64). Accordingly, **Fabijanski et al. do not disclose a plant selection strategy that is not based on antibiotic resistance.** Rather, Fabijanski et al. teach away from such a strategy in their demonstration of selection using a kanamycin resistance gene.

The Office Action states:

*Further, Applicants argue that pCG-2 transformation vector includes a kanamycin resistance gene, which teaches away from instant invention (response, page 7, 2<sup>nd</sup> paragraph).*

*The Office contends that Fabijanski et al. still teach all the limitations set forth by the claims and none of the first, second and third coding regions encode proteins conferring kanamycin resistance.*

Claims 1 and 14 have been amended to remove reference to the first, second and third coding regions encoding proteins that are not antibiotic resistant, and instead now define that the whole plant selection strategy is not based on antibiotic resistance. Fabijanski et al. use of antibiotic resistance as a selection marker, teaches away from the presently claimed invention.

The addition of Mason et al. and Chou et al. do not remedy the deficiencies of Fabijanski et al. More specifically, Mason et al. teach transgenic tobacco plants expressing the hepatitis B surface antigen under the control of CaMV 35S promoter and Chou et al. teach the zinc finger gene from *agrobacterium*, *ros*, and repression of the *virC/D* and *ipt* genes by binding of *ros* to the conserved operator “*ros box*”. However, even if the hepatitis B surface antigen of Mason et al. and the *ros* operator of Chou et al. were combined with the genetic constructs taught by Fabijanski et al., the skilled person would still not arrive at the claimed invention without having recourse to the disclosure of the above-referenced application since, to make the combination, the skilled person would have to ignore the specific teachings of Fabijanski et al. that the coding sequence encoding the tag protein is a lethal gene, such that expression of the nucleotide sequence containing the coding region for the tag protein results in a non-viable plant and that antibiotic resistance is a suitable selection strategy. With respect, this is impermissible hindsight reconstruction.

Accordingly, the Applicants respectfully submit that the combination of Mason et al. and Chou et al. with Fabijanski et al. do not lead to the claimed invention, particularly in view of Fabijanski et al.’s teaching of providing a lethal gene on each transformation construct and endorsement of antibiotic resistance. The Applicants therefore respectfully request that this rejection be withdrawn.

### **Double Patenting**

Claims 1-8, 10 and 14 remain provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 18-24 of copending Application No. 10/719,996 (now issued as US 7,321,077) in view of Mason et al. Applicants respectfully traverse the double patenting rejection.

Claims 18 and 24 of Application No. 10/719,996 were withdrawn and are not present in US 7,321,077. Claim 19 (issued claim 1) describes a method involving two constructs: one comprising a regulatory region driving the expression of a gene of interest and a ROS operator controlling the activity of the regulatory region. The second construct comprises a regulatory region driving the expression of a ROS repressor. Claim 1 reads as follows:



1. A method for selectively controlling the transcription of a gene of interest in a plant, comprising:

- i) producing a first plant comprising a first genetic construct, said first genetic construct comprising a first regulatory region operatively linked to a gene of interest and one, or more than one, ROS operator sequence capable of controlling the activity of said first regulatory region;
- ii) producing a second plant comprising a second genetic construct, said second genetic construct comprising a second regulatory region in operative association with a nucleic acid molecule encoding an *Agrobacterium* ROS repressor optimized for expression in a plant, said ROS repressor exhibiting both ROS operator binding activity and ROS repressor activity;
- iii) crossing said first plant and said second plant to obtain progeny, said progeny comprising both said first genetic construct and said second genetic construct, and characterized in that the expression of said second genetic construct represses expression of said first genetic construct.

The constructs defined in claim 1 of US 7,321,077 are different both in composition and in function when compared to the constructs of the present invention. The first construct of the present invention comprises a sequence encoding a tag protein, and does not comprise a gene of interest as defined in claim 1 of US 7,321,077. Rather, in the construct of the present invention, the gene of interest is located on the second construct. The second construct also comprises a sequence that encodes a repressor.

Claim 2 of US 7,321,077 (old claim 20) depends from claim 1 and defines alternate promoters. Claims 3-5 of US 7,321,077 (old claims 21-23), comprise similar components in the constructs as outlined in claim 1 above, and differ in the promoter used.

Mason et al. teach transgenic tobacco plants expressing the hepatitis B surface antigen under the control of CaMV 35S promoter and this reference does not provide any guidance to use the combination of elements in the constructs as claimed in claims 1-8, 10 and 14.

Therefore, Applicant submits that the claims 1-8, 10 and 14 of the present application are not an obvious variation over claims 18-24 of Application No. 10/719,996 (US 7,321,077).

Claims 1-8, 10 and 14 remain provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 18, 21 and 24 of Application No. 10/995,951 (now issued as US 7,521,595) in view of Mason et al. Applicants respectfully traverse the double patenting rejection.

Claim 24 of Application No. 10/995,951 was withdrawn and it is not present in US 7,521,595. Claim 18 (now claim 11 as issued in 7,521,595) is dependent on issued claim 9 and 1. Issued claim 11 describes a method involving two constructs: one comprising a regulatory region driving the expression of a gene of interest and a ROS operator controlling the activity of the regulatory region. The second construct comprises a regulatory region driving the expression of a ROS repressor. Issued claim 11, 9, and 1 read as follows:

11 . The plant of claim 9, wherein said gene of interest encodes a protein selected from the group consisting of one or more enzymes involved in fiber biosynthesis, one or more enzymes involved in glucosinolate biosynthesis, one or more enzymes involved in phytotoxin biosynthesis, caffeic o-methyltransferase, indole acetamide hydrolase, and phosphinothricin acetyl transferase.

9. A plant comprising;
- i) a first genetic construct comprising a genetic construct comprising a regulatory region operatively linked to a gene of interest and one, or more than one, ROS operator sequence capable of controlling the activity of said regulatory region, wherein said regulatory region is functional in plants, and
  - ii) a second genetic construct comprising a regulatory region in operative association with the nucleic acid molecule of claim 1.
1. A nucleic acid molecule encoding a ROS repressor optimized for plant codon usage and exhibiting ROS operator binding activity, ROS repressor activity, or both ROS operator binding activity and ROS repressor activity, wherein said nucleic acid molecule comprises the nucleotide sequence of SEQ ID NO: 2 or SEQ ID NO: 3.

The constructs defined in claim 9 of US 7,521,595 are different both in composition and in function when compared to the constructs of the present invention. The first construct of the present invention comprises a sequence encoding a tag protein. The first construct does not comprise a gene of interest as defined in claim 1 of US 7,521,595. Rather, in the

construct of the present invention, the gene of interest is located on the second construct. The second construct also comprises a sequence that encodes a repressor.

Mason et al. teach transgenic tobacco plants expressing the hepatitis B surface antigen under the control of CaMV 35S promoter and this reference does not provide any guidance to use the combination of elements in the constructs as claimed in claims 1-8, 10 and 14.


Therefore, Applicant submits that the claims 1-8, 10 and 14 of the present application are not an obvious variation over claims 18, 21 and 24 of Application No. 10/995,951 (US 7,521,595).

### **CONCLUSION**

Applicants believe that the application is now in good and proper condition for allowance. Early notification of allowance is earnestly solicited.

Respectfully submitted,

Date: September 11, 2009

  
\_\_\_\_\_  
Viola T. Kung, Ph.D. (Reg. No. 41,131)

HOWREY LLP  
2941 Fairview Park Drive, Box 7  
Falls Church, VA 22042  
Tel: (650) 798-3570  
Fax: (650) 798-3600